Attachment 1. Date 23 JAN 82

ETHICAL REVIEW COMMITTEE, ICDDR,B. 88

Principal Investigator DR BRIAN SEATON Trainee Investigator (if any) —

Application No. 82-004 Supporting Agency (if Non-ICDDR,B) —

Title of Study EFFECT OF NUTRITIONAL STATUS ON THE PHARMACOKINETICS OF DEPO MEDROXYPROGESTERONE ACETATE

Project status:
(✓) New Study
( ) Continuation with change*
( ) No change (do not fill out rest of form)

Circle the appropriate answer to each of the following (If Not Applicable write NA).

1. Source of Population:
   (a) Ill subjects — Yes (No)
   (b) Non-ill subjects — (Yes) No
   (c) Minors or persons under guardianship — Yes (No)
2. Does the study involve:
   (a) Physical risks to the subjects — Yes (No)
   (b) Social Risks — Yes (No)
   (c) Psychological risks to subjects — Yes (No)
   (d) Discomfort to subjects — (Yes) No
   (e) Invasion of privacy — Yes (No)
   (f) Disclosure of information damaging to subject or others — Yes (No)
3. Does the study involve:
   (a) Use of records, (hospital, medical, death, birth or other) — Yes (No)
   (b) Use of fetal tissue or abortus — Yes (No)
   (c) Use of organs or body fluids — (Yes) No
4. Are subjects clearly informed about:
   (a) Nature and purposes of study — (Yes) No
   (b) Procedures to be followed including alternatives used — (Yes) No
   (c) Physical risks — (Yes) No
   (d) Sensitive questions — ~~Yes No~~ N/A
   (e) Benefits to be derived — (Yes) No
   (f) Right to refuse to participate or to withdraw from study — Yes No
   (g) Confidential handling of data — (Yes) No
   (h) Compensation &/or treatment where there are risks or privacy is involved in any particular procedure — ~~Yes No~~ N/A
5. Will signed consent form be required:
   (a) From subjects — (Yes) No
   (b) From parent or guardian (if subjects are minors) — ~~Yes No~~ N/A
6. Will precautions be taken to protect anonymity of subjects — (Yes) No
7. Check documents being submitted herewith to Committee:
   — Umbrella proposal - Initially submit overview (all other requirements will be submitted with individual studies).
   ✓ Protocol (Required)
   ✓ Abstract Summary (Required)
   ✓ Statement given or read to subjects on nature of study, risks, types of questions to be asked, and right to refuse to participate or withdraw (Required)
   ✓ Informed consent form for subjects
   N/A Informed consent form for parent or guardian
   ✓ Procedure for maintaining confidentiality
   ✓ Questionnaire or interview schedule *

* If the final instrument is not completed prior to review, the following information should be included in the abstract summary:
1. A description of the areas to be covered in the questionnaire or interview which could be considered either sensitive or which would constitute an invasion of privacy.
2. Examples of the type of specific questions to be asked in the sensitive areas.
3. An indication as to when the questionnaire will be presented to the Cttee. for review.

We agree to obtain approval of the Ethical Review Committee for any changes involving the rights and welfare of subjects before making such change.

Brian Seaton
Principal Investigator

Trainee

SECTION I - RESEARCH PROTOCOL

1) Title : Effect of Nutritional Status on the Pharmacokinetics of Depo-Medroxy Progesterone Acetate.

2) Principal Investigator : Dr. Brian Seaton (ICDDR,B)
Dr. Dianne Riad-Fahmy (Tenovus Inst.)

3) Starting Date : February 1982

4) Completion Date : November 1982

5) Total Direct Cost : $ 11,769

6) Scientific Program Head:

This protocol has been approved by the Community Services Research Working Group.

W. J. [signature]
Signature

21/1/82
Date

7) Abstract Summary

Nutritional status would be expected to affect the pharmacokinetics of Depo Medroxy Progesterone Acetate (DMPA). However, there have been no well-designed studies to investigate the extent to which nutritional status, particularly chronic malnutrition as exist in many areas of Bangladesh, affects the kinetics and pharmacology of DMPA use and the implications of such effects in terms of the widespread use of DMPA as a contraceptive. This study will investigate this issue.

8) Reviewers

(a) Research Involving Human Subjects _____

(b) Research Review Committee _____

(c) Director _____

(d) BMRC _____

(e) Controller/Administrator _____

SECTION II - RESEARCH PROTOCOL

A. INTRODUCTION

1. Objective

To determine the effects of nutritional status on the Pharmacokinetics of Depo-Medroxy Progesterone Acetate (DMPA) in rural Bangladeshi women.

2. Background

Like most hormonal contraceptives, depo-medroxy progesterone acetate (DMPA) was largely developed and tested in the developed countries of the west, notably the USA. However, DMPA is now widely used in the less-developed countries where chronic malnutrition is wide-spread, particularly amongst the rural women of low socio-economic status who from the most important target-group for family-planning programs. It is therefore pertinent to enquire whether such chronic malnutrition affects the pharmacology of DMPA in such populations and, if so, whether this has any significance to the use of DMPA in such populations.

"Chronic malnutrition" is a very broad term which describes a wide variety of conditions, some more specifically definable than others, and not all of which are even closely related to each other. Specific dietary deficiencies may give rise to specific, readily identifiable conditions (eg. scurvey, Anemia, kwashikor, etc.) whereas a meagre diet may be very non-specific and/or rather variable in its effects.

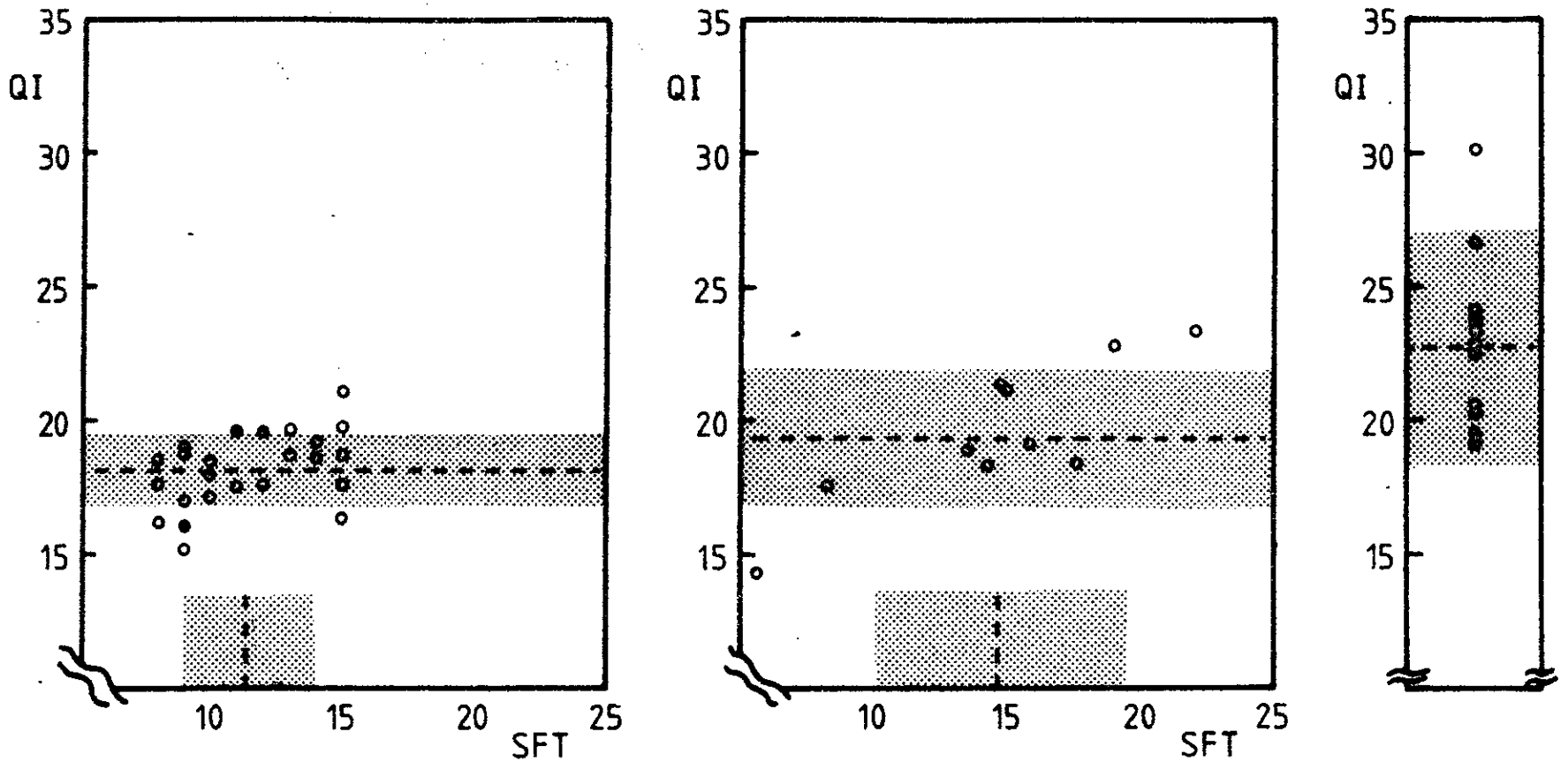
Relatively little is known about the metabolism of DMPA in humans (Fotherby, 1973; Fraser, 1981). Following the administration of radioisotopically labelled medroxy-progesterone acetate intravenously only a small proportion is recovered in urine (20-42%) and faeces (3-15%) (Slaunwhite & Sandberg, 1961; Fotherby et al, 1968; quoted by Fotherby 1973). Despite these low recoveries, the same authors also found a rapid disappearance of radioactivity from the

blood-stream, the initial half-life was 52 mins, the second half-life was 230 mins, only 15-2.5% of the dose was present in the total plasma volume after 4 hrs and by 12 hrs no radioactivity at all could be detected. These data suggest that medroxy progesterone acetate may rapidly distribute into other body tissue, eg. body fat.

There are no known reports of specific requirements (eg. co-factors) for the metabolism of DMPA in humans, hence there are no known dietary deficiencies which specifically affect the pharmacokinetics of DMPA. However, chronic malnutrition could affect the pharmacokinetics of DMPA through a number of possible mechanisms:- (a) DMPA is a relatively non-polar molecule, more soluble in non-polar organic solvents than in aqueous solvents, hence the body fat compartment could play a significant role as a buffer or reservior for DMPA, as previously suggested; (2) nutritional status may affect the rate of release of DMPA from the injection site by affecting the realtive obesity, muscularity and vascularity of the injection site; (3) despite the lack of detailed information it seems likely that DMPA is metabolised and conjugated in the liver before being excreted (like most other steriods there is probably a significant enterohepatic circulation) and these could be affected by chronic malnutrition.

Whilst there have been a number of studies on the pharmocokinetics of DMPA (see Fotherby, 1973; Fraser, 1981; for reviews) there have been no published detailed studies of the effects of nutritional status on the pharmacokinetics of DMPA (Fotherby et al, 1980; see *footnote). A recent study by Fotherby et al (1980) on the pharmacokinetics of DMPA in Thai women of "low" body-weight did not really address the effects of nutritional status since the only anthropometric determination made was of quetelet's Index (Khosla and Lowe, 1967; quoted by Fotherby), weight/height^2, and, as can be seen from figure 1, the QI values for the Thai subjects were

* A letter has been sent to the Upjohn Co. requesting them to supply any data that they may have on the effects of nutritional status on the pharmacokinetics of DMPA. Any relevant information will be appended to this protocol when received.



Key ○ Single observations ● Multiple observations mean ± 1s.d.

QI Quetelet's Index *(wt/ht²; kg/m²)* SFT Skin-Fold Thickness *(mm)*

Anthropometric Measurements from Different Studies

comparable to those from women in developed countries and some subjects were frankly obese (see Garrow, 1979). By contrast, the QI value of women of low socio-economic status in Nandepare, an ICDDR,B field area on the outskirts of Dacca, Bangladesh (Seaton, unpublished data) and in Hyderabad, India (Prasad et al; Nair et al, 1979) is markedly lower (Figure 1).

Fortherby et al (1980) state :-

> "Almost all of the pharmacokinetic studies of Depo-Provera have been carried out in Caucasion women and it might be expected that in other ethnic groups, usually of lower body-weight, the dose of Depo-Provera could be considerably reduced without any loss of efficacy".

This seems to be an inherently reasonable proposition; indeed one can go further and hypothesise that regimes of DMPA optimised on the basis of data obtained from well-nourished women in developed countries may be inappropriate for chronically malnourished women having marked differences in the relatives sizes of the various body compartments, thereby increasing their susceptibility to undesirable side effects. Significant effects of chronic malnutrition on the pharmacokinetics of the synthetic steroids used in oral contraceptives have been reported from India(Prasad et al, 1979; Nair et al, 1979). It was interesting to note that it was the size of the deep compartment (which can very reasonably be ascribed to body-fat) in the classical 3-compartment model which was found to be highly correlated with skin-fold thickness and become zero in women with very low skin-fold thickness. Unfortunately, the Fotherby (1980) study was not adequately designed to resolve the effects of nutritional status on the pharmacokinetics of DMPA and so the question remains unanswered.

A particular problem of attempting a study on the pharmacokinetics of DMPA in Bangladeshi women, particularly those of low socio-economic status, is their reluctance to give blood samples for

research programmes. This stems from a variety of cultural beliefs, many of them eroneous, about the nature and function of blood in the body (eg. some people believe that blood is not replaced by the body so that any blood lost or withdrawn is a permanent loss). In order to overcome this, the protocol will commence with a small study to validate the determination of DMPA in saliva as a proxy measure of DMPA in blood. There have been a large number of studies on the use of saliva as an alternative to blood for determining a wide variety of substances (eg. cortisol, Katz & Shannon, 1969; Walker et al., 1978; Cambell et al., 1981: testosterone, Wang et al., 1981; Walker et al., 1978: estrogen, Gombie, 1977: progesterone, Gombie, 1977; Walker, 1981; Walker, 1979; Seaton & Fahmy, 1980: 17a-hydroxprogesterone, Walker & Fahmy, 1978: to quote just a few). So far as is known there have been no studies on the use of saliva for the determination of DMPA, but DMPA is known to appear in the milk of lactating mothers who receive DMPA as a contraceptive and the milk (plasma concentration ratio is 1:1 (Saxena et al, 1977) suggesting that there is no significant protein binding of DMPA in the blood. This gives us every reason to believe that saliva will provide a practical alternative to blood for monitoring the pharmacokinetics of DMPA.

3) Rationale

Back et al. (1981) state :-

> "Dietary factors play an important role in regulating human drug metabolism. Changing the ratio of protein to carbohydrate in the diet, feeding a diet which contains charcoal-broiled beef or feeding a diet which contains large amounts of cabbage or Brussels sprouts all influence human drug metabolism (Canney et al., 1979). With oral contraceptives steroids prescribed world-wide in similar doses we could expect to find considerable differences in the handling of the steroids in well-nourished/malnourished women and in vegetarian/non-vegetarian women".

The same is potentially true of DMPA. However, unlike oral contraceptives which are distributed in pill form and therefore much less amenable to adjustment of the dose to suit the metabolic characteristics of individual acceptors, DMPA is distributed as an intramuscular injection and it would be extremely easy to vary the dose to suit the individual if an appropriate algorithmn were available.

A study of the pharmacokinetics of DMPA in relation to nutritional status might result in such an algorithmn in addition to producing more basic information on the use of DMPA in such populations.

B. SPECIFIC AIMS

To determine the effects of nutritional status on the Pharmacokinetics of Depo-medroxy Progesterone Acetate (DMPA) in rural Bangladeshi women.

C. METHODS OF PROCEDURE

Phase 1: Validation of Saliva Assays for DMPA

Six to nine subjects, purposefully selected to be two or three each of low, medium and high nutritional status (defined for purposes of this study on the basis of mid-arm skin-fold thickness: low-group less than 10mm skin-fold; medium-group 10-15mm; high-group more than 15mm skin-fold from DMPA) acceptors in either Dacca or Matlab areas as appropriate will be selected. 3 ml saliva and 5 ml blood samples will be collected by standard proceudres according to the following schedule: (1) immediately prior to the DMPA injection; (2) 2 days after the DMPA injection; (3) one week after the DMPA injection; (4) two weeks after the DMPA injection; (5) 4 weeks after the DMPA injection.

The blood samples will be allowed to clot at ambient temp., the serum will then be withdrawn and deep-frozen. The saliva will be deep-frozen as soon as possible after collection. The first and last samples (1 & 5) of both blood and saliva will be tested for the presence of Hepatitis B Surface Antigen by a standard commercial kit (eg. Hepanosticon from Organon).
The deep-frozen samples will be transported by air-freight (subject to Governmental and IATA regulations concerning the shipment of medical specimens for research) to the Tenovus Institute, Welsh National School of Medicine, Cardiff, UK. for assay for DMPA by RIA. The correlation between saliva and serum concentrations of DMPA will be established by the usual statistical procedures.

C. Phase 2: Pharmacokinetics of DMPA

15-24 apparently normal DMPA acceptors aged 20-35 in the Matlab MCH-FP program will be purposefully selected to be 5 to 8 each of low, medium and high nutritional status (as previously defined). Preference will be given to recruiting new acceptors of DMPA; clients who have used OCs within the previous 18 months will be excluded, as will any clients with frank clinical problems. 3ml saliva will be collected from each subject according to the following tentative* schedule :- (1) immediately prior to the injection of DMPA; (2) 4 hrs after the injection; (3) 24 hrs after; (4) 3 days; (5) 1 week; (6) 2 weeks; (7) 1 month; (8) 2 months; (9) 3 months (ie. immediately prior to the next injection). Subjects will be studied over two concecutive injections of DMPA.

At monthly intervals saliva samples will be tested for Hepatitis B surface antigen (commercial kit) prior to being deep-frozen. Samples will be stored at $-20^{\circ}C$ until analysed.

Anthropometric Determinations

All subjects (both Phase 1 and Phase 2) will be examined for (1) height, (2) weight, (3) mid-arm circumference, (4) mid-arm skin fold thickness (3 & 4; both left and right arms) at the beginning of the study, prior to each injection of DMPA and at the end of the study.

Data Analysis

The data obtained in phase 1 will establish the validity of salivary DMPA assays as a proxy determination of blood DMPA levels. Linear regression coefficients will be calculated by the reduced major axis procedure (Kermack & Haldane, 1980) and correlation coefficients calculated in the usual way.

The execution of Phase 2 will be dependent upon the successful completion of Phase 1.

The data obtained in Phase 2 will be analysed using standard multi-compartmental pharmacokinetic models employing non-linear least-squares curve-fitting procedures on the IBM S/34 computer, (eg. McIntosh & McIntosh, 1980; Tait, 1970). The pharmacokinetic parameters will be correlated with the anthropometric data by the usual statistical methods. The results will, if appropriate, be stratified according to whether the subjects are vegetarian or non-vegetarian.

D. SIGNIFICANCE

Information about the effects of chromic ill-health or malnutrition are of crucial importance to the development of appropriate contraceptive programmes in Bangladesh and other less-developed countries. The data obtained in this study may be of direct benefit by providing guidelines for the selection of individually optimised does of DMPA for each subject.

E. FACILITIES REQUIRED

Existing office and laboratory space for the principal investigator are adequate. Out-patient facilities may be required for the collection of samples during Phase-1 only. In-patient and animal facilities are not required. Logistic support will be required for subjects in Phase-1 and for field-staff in Phase-2. All major items of equipment required to establish DMPA RIA in Dacca are currently available. Access to the S/34 computer will be required for processing the Data. However, some of the initial work in establishing the required programmes on the IBM S/34 computer has already been done.

F. COLLABORATIVE ARRANGEMENTS

During Phase-1 DMPA RIA will be done at the Tenovus Institute, Cardiff. The ICDDR,B will bear the costs of collecting and shipping the samples and the Tenovus Institute will bear the costs of

developing the RIA and assaying the samples. For Phase-2 a decision will be made on the basis of the Phase - 1 experiences and results whether to continue assaying the samples in Cardiff or to establish the DMPA RIA in Dacca. Data analysis will be done both in Dacca and Cardiff and all publications will be joint authorship.

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SECTION III - BUDGET

A. DETAILED BUDGET

1) Personnel Services

Sl. No.	Name	Position	Monthly Rate	Person Months	Estd.Cost 1982
1	Dr Brian Seaton+	Scientist	$3000	10x0.1	3000
2	To be named*	Sr.Field Asst.	Tk3536	10x0.5	1105
3	To be named	Programmer	Tk5592	3x0.1	105
					4210

Notes: +See comment in budget summary
*Should be same person as named in Oral Contraceptive Compliance stud

2) Travel & Transportation of Persons

B. International

Sl.No.	Name	Particulars	No Days	Estd.Cost 1982
EITHER	Dr Brian Seaton	Travel to UK to collaborate with Tenovus Inst. staff.	10	3500
OR	Member of Tenovus staff	Travel to ICDDR,B to establish DMPA RIA	20	

3) Transport of Materials

c)	Other: Shipment of samples to UK, 3x20kg	400

4) Rent, Communication & Utilities

a)	Communication:	200

5) Printing & Reproduction

a)	Printing of forms (mimeography)	50
d)	Xeroxing	50

6) Other Contractual Services

a)	Computer services:	
	Terminal time, 40x10hrs/wk @ Tk20/hr	500
	Computer time (for programmer)	650
	Lineprinter output	100
		1250
b)	Daily wager:	
	Boatman, Matlab, 40x20hrs/wk @ Tk2.75/hr	140

7) Supplies & Materials

h)	Office supplies & stationery	100
i)	Misc., Gifts to subjects, 30 @ $10	300
		400

		Estd.Cost 1982
8)	Equipment	nil
9)	Transport	
	a) ICDDR,B transport in Dacca	100
	b) Trips to Matlab, 10trips @ Tk270/trip	169
	c) Speedboat, Matlab 24x5hrs/wk @ Tk200/hr	1500
		1769
10)	Patient Hospitalisation	nil
11)	Outpatient Care (Covered under FP-MCH protocol)	nil

12) Laboratory Tests

Sl. No.	Particulars	No. Tests	Rate	Estd.Cost 1982
1	DMPA RIA (if required in Phase-2)	20x24	$5	2400
2	Hepatitis B surface antigen	100	$4	400
				2800

13)	Construction, Renovation & Alterations	nil
14)	Income	nil

B. SUMMARY BUDGET

Sl. No.	Category	Estd.Cost 1982
1	Personnel Services.	4210+
2	Travel & Transportation of Persons	3500
3	Transport of Materials	400
4	Rent, Communication & Utilities	200
5	Printing & Reproduction	100
6	Other Contractual Services	1390
7	Supplies & Materials	400
8	Equipment	-
9	Transport	1769
10	Patient Hospitalisation	-
11	Outpatient Care	-
12	Laboratory tests	2800
13	Construction, Renovation & Alteration	-
14	Income	-
	TOTAL COST 1982	$14,769+

Note: + Dr Seaton's salary is paid directly by the ODA and does not pass through the ICDDR,B accounting procedures. The nominal figure of $3000 is included to reflect the real cost of the protocol, but the actual cost to ICDDR,B is $3000 less.

ABSTRACT SUMMARY FOR ETHICAL REVIEW COMMITTEE

1) This protocol specifically studies the pharmacokinetics of Depo-Medroxy-Progestrone-Acetate (DMPA) in Bangladeshi women under typical environmental conditions. Animals cannot therefore be used as an alternative.

2) All the subjects will be volunteers who have decided of their own accord to accept DMPA as a contraceptive agent; ie. DMPA will not be administered for the purpose of this study to any person who, were it not for the study, would not otherwise have received DMPA.

In Phase-1, the only risk to the subject is the negligible risk associated with venepuncture for the purpose of drawing blood. In Phase-2 there is no risk at all to the subject as only saliva will be collected. The study will not generate any potentially embarasing data.

3) Venepuncture, the only potential risk in the study, will be done by experienced personnel using standard aseptic techniques.

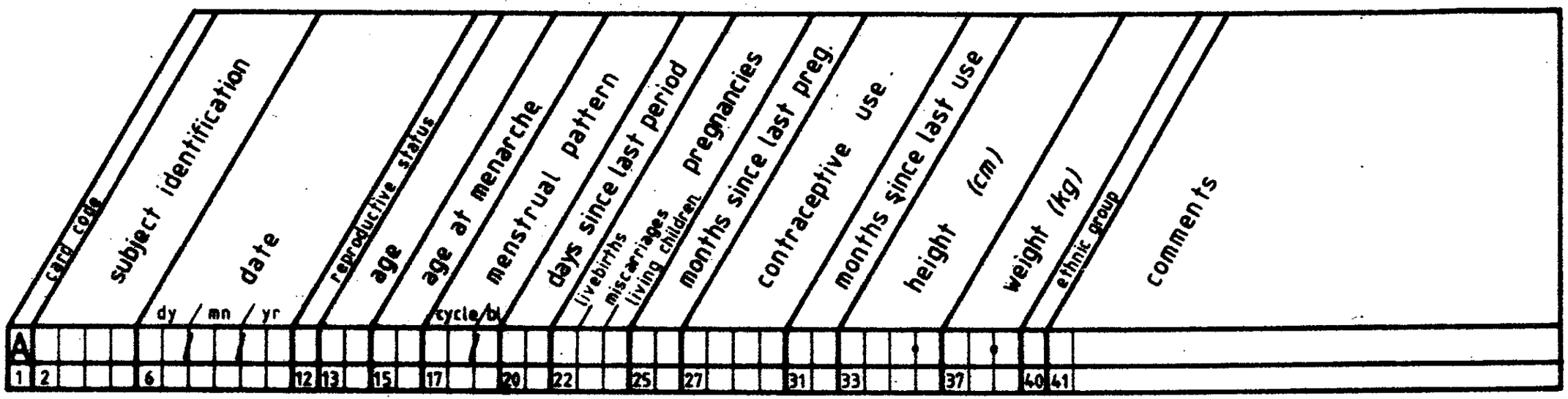
4) Data will be held in locked files in the office of the Pricipal Investigator. Subjects will not be identified by name to any person not directly concerned with the study, nor in any publication arising from the study.

5) Written consent will be obtained in both Phase-1 and Phase-2 of the study.

6) The study requires only the collection of basic reproductive history on the standard Endocrinology Study admission form (attached) with the addition of the following question:- "Are you a vegetarian, eating neither meat nor fish?" (Answer, Yes or No). Estimated time required for completing the admission form is 1-2minutes.

7) The subjects will not receive any direct health benefit from participating in this study. However, society as a whole will benefit from a better understanding of the effects (if any) of chronic malnutrition on the use of DMPA. Subjects participating in the study may be offered a small gift (eg. a sari) at a value of approx. US$10 (Tk150-200) as a compensation for the inconvenience of participating in the study.

8) The study requires the use of blood and saliva in Phase-1 and saliva only in Phase-2. Other body fluids, or the use of medical records, will not be required.



Subject's name _____ Census no. _____

ICDDR,B Endocrinology Study BS 2/79 A-3

CONSENT FORM - PHASE 1

The ICDDR,B., as part as its policy of trying to improve the quality of its services to the community, is undertaking a study to see whether nutritional status (i.e. whether you are big or small, fat or thin) has any effect on the use of Depo Provera as a contraceptive agent. Although this study will not benefit you immediately, you may benefit later if we find that a different dose of DMPA is better for a person with your body size.

In order to do this study we need to collect samples of saliva and blood (approximately 1 tea-spoon full of each) on five occasions:-

1) immediately before you receive the injection of DMPA
2) 2 days after receiving the injection
3) 1 week after the injection
4) 2 weeks after the injection
5) 4 weeks after the injection.

The ICDDR,B will come to your house to collect the sample or provide you with the necessary transport for you to come to our hospital to give the samples. Apart from the small inconvenience of having to return to the hospital and the minor discomfort of giving a blood sample there is no risk to you in participating in this study since your body will quickly replace the blood which we take and our staff are very skilled at minimising your discomfort.

To compensate you for your inconvenience and discomfort we will offer you a small gift if you complete the study.

You may ask any questions you wish about this study either before agreeing to participate or after. You are not obliged to help us in this way or, if you agree at first and then change your mind later you may refuse to help us any further. In either case it will not

create any problem for you and you will continue to receive all the normal services.

The imformation which we collect will be kept confidential and no person, other than those directly concerned with the study, will come to learn that you helped us in this study.

Subject's Consent

I understand the information given above. I have been given the opportunity to ask any questions that I wish and I am satisfied with the answers I have received.

I agree to participate in the study.

_____ _____ _____

CONSENT FORM - PHASE 2

The ICDDR,B., as part as its policy of trying to improve the quality of its services to the community, is undertaking a study to see whether nutritional status (i.e. whether you are big or small, fat or thin) has any effect on the use of Depo Provera as a contraceptive agent. Although this study will not benefit you immediately, you may benefit later if we find that a different dose of DMPA is better for a person with your body size.

In order to do this study we need to collect samples of saliva on eighteen occasions:-

1) immediately before you receive the injection of DMPA
2) 4 hrs. after receiving the injection
3) 24 hrs after the injection
4) three days after the injection
5) 1 week after the injection
6) 2 weeks after the injection
7) 1 month after the injection
8) 2 months after the injection
9) 3 months after the injection (i.e. immediately before the next injection).

The above schedule will then be repeated up to the time of your next injection when our study will stop (though you may, of course, continue to receive the contraceptive if you wish).

The ICDDR,B will come ot your house to collect the sample or provide you with transport for you to come to the hospital to give the samples. Apart from the minor inconvenience to you of giving the samples, participating in this study will not create any problem for you.

You may ask any questions you wish about this study either before agreeing to participate or after. You are not obliged to help us in this way or, if you agree at first and then change your mind

later you may refuse to help us any further. In either case it will not create any problem for you and you will continue to receive all the normal services.

The information which we collect will be kept confidential and no person, other than those directly concerned with the study, will come to learn that you helped us in this study.

Subject's Consent

I understand the information given above. I have been given the opportunity to ask any questions that I wish and I am satisfied with the answers I have received.

I agree to participate in the study.

_____ _____ _____

সম্মতি - পত্র - ১

পল্লীজনগণের সেবা - মান উন্নয়নের জন্য বাংলাদেশে আন্তর্জাতিক উদরাময় গবেষণা কেন্দ্র নীতিগতভাবে প্রচেষ্টা চালিয়ে যাচ্ছে। এইজন্য একটি গবেষণা কর্মসূচি হাতে নেওয়া হয়েছে। এতে "ডেপো প্রভেরা" জন্ম নিরোধ দ্রব্য হিসাবে ব্যবহারের উপর আপনার দেহে সুবিধা (আপনি মোটা অথবা পাতলা, দুর্বল বা বড়) কোন প্রকার প্রভাব আছে কিনা দেখে দেখা হবে। অবশ্য আপনি সাথে সাথে এই গবেষণা থেকে উপকৃত হবেন না। তার পরবর্তী সময় একটি লোকের উপর শারীরিক মাপের জন্য বিভিন্ন পরিমাণের "ডেপো প্রভেরা" ব্যবহারে সুফল পেতে পারেন।

তাই এই প্রচেষ্টা বাস্তবায়িত করার জন্য আমাদের অল্প কিছু লালা ও রক্ত (চা চামচের একচামচ) নেবার প্রয়োজন হবে এবং নিম্ন নির্দিষ্টভাবে সংগ্রহ করতে হবে।

১ ডেপো প্রভেরা ইনজেকশন ব্যবহার করার অব্যবহিত আগে,
২ ইনজেকশন নেওয়ার দুই দিন পর
৩ ইনজেকশন নেওয়ার এক সপ্তাহ পর
৪ ইনজেকশন নেওয়ার দুই সপ্তাহ পর
৫ ইনজেকশন নেওয়ার দুই সপ্তাহ পর।

আন্তর্জাতিক উদরাময় গবেষণা কেন্দ্র এই লালা ও রক্ত সংগ্রহের জন্য আপনার বাড়িতে আসিবে অথবা আপনাকে হাসপাতালে যাওয়ার জন্য প্রয়োজনীয় গাড়ীর ব্যবস্থা করিবে। যদিও হাসপাতালে আসিতে এবং রক্ত দিতে আপনার একটু অসুবিধা হইবে, কিন্তু এই রক্ত দেওয়াতে আপনার স্বাস্থ্যের উপর কোন ক্ষতিকর

আসবে না। এই রক্ত অথবা সময় আপনার শরীরে স্বাভাবিক ভাবে পূরণ হয়ে যায়, তাছাড়া আমাদের দক্ষ কর্মচারীরা আপনার অসুবিধা যাতে না হয় তার প্রতি যত্ন নিতে তৎপর থাকবে। তাই এই গবেষণায় অংশ গ্রহণ করাতে আপনার ভয়ের কিছু নেই।

যদি আপনি এই প্রকল্পে শেষ পর্যন্ত সহযোগীতা করেন, তবে আমরা আপনাকে আপনার এই অসুবিধার জন্য কিছু উপহার-সামগ্রী প্রদান করব।

যদি ইচ্ছা করেন তবে এই প্রকল্পে অংশগ্রহণ করবার আগে ও পরে যে কোন প্রশ্ন জিজ্ঞাসা করতে পারেন। আমাদেরকে এই উপায় সাহায্য করতে আপনার কোন বাধ্যবাধকতা নেই। আপনি যদি প্রথমত: স্বীকার করেন ও পরে মত পরিবর্তন করেন যে আমাদিগকে সাহায্য করা আপনার জন্য সম্ভব নয় তবেও কিছু যায় আসে না। এতে আপনার জন্য কোন সমস্যা হবে না এবং আপনি ঠিকমতই প্রকল্পের সুযোগ সুবিধা পাবেন।

সমস্ত তথ্যাবলীর পূর্ণ গোপনীয়তা রক্ষা করা হবে এবং যারা এই প্রকল্পের সাথে ওতপ্রোতভাবে জড়িত আছে শুধু তাহারাই জানতে পারবে যে আপনি আমাদেরকে এই প্রকল্পে সাহায্য করেছেন।

<u>সম্মতি-বিষয়বস্তু</u>

উল্লেখিত তথ্যাবলী আমি বুঝিয়াছি, আমি যে কোন প্রশ্ন জিজ্ঞাসা করবার সুযোগ পেয়েছি আমি আশা করি যে আমি আমার প্রশ্নের সন্তোষজনক উত্তর পেয়েছি এবং এই প্রকল্পে অংশ গ্রহণ করতে স্বীকার করলাম

সম্মতি পত্র - 2

পল্লী জনগণের সেবার মান উন্নয়নের জন্য বাংলাদেশের আন্তর্জাতিক উদরাময় গবেষণাগার নীতিগত ভাবে প্রচেষ্টা চালিয়ে যাচ্ছে। এইজন্য একটি গবেষণা কর্মসূচী হাতে নেওয়া হয়েছে। এই প্রকল্পে "ডিপো প্রভেরা" জন্ম নিরোধ দ্রব্য হিসাবে ব্যবহার করার উপর আপনার দেহের ঋতুস্রাব (অর্থাৎ আপনি কম অথবা বেশী, মোটে অথবা দাগলে) কোন প্রকার প্রভাব আছে কিনা দেখা হবে। অবশ্য আপনি সাথে সাথে এই গবেষণা থেকে উপকৃত হবেন না। তবে পরবর্তী সময়ে একটি লোকের শারীরিক মাসিক উপর বিভিন্ন মাত্রার ডেপো প্রভেরা ব্যবহারের সুফল পেতে পারেন।

তাই এই প্রকল্প বাস্তবায়িত করার জন্য আপনাদের অল্প কিছু লালা ও রক্ত প্রয়োজন মত নিম্নলিখিত ভাবে আপনার সংগ্রহ করার দরকার:

① ডেপো প্রেভেরা ইনজেকশন ব্যবহার করার - অন্তর্ভুক্তির আগে।
② ইনজেকশন নেওয়ার ৪ ঘণ্টা পর -
③ ইনজেকশন নেওয়ার 24 ঘণ্টা পর -
(৪) ইনজেকশন নেওয়ার ৩ দিন পর -
(৫) ইনজেকশন নেওয়ার ১ সপ্তাহ পর -
(৬) ইনজেকশন নেওয়ার 2 সপ্তাহ পর -
(৭) ইনজেকশন নেওয়ার ১ মাস পর -
(৮) ইনজেকশন নেওয়ার 2 মাস পর -
(৯) ইনজেকশন নেওয়ার ৩ মাস পর (অর্থাৎ পরবর্তী ইনজেকশন নেওয়ার আগে)

যখন আপনাদের প্রকল্প শেষ হবে তখন আপনার পরবর্তী ইনজেকশন পাওয়া পর্যন্ত উল্লিখিত তালিকার পুনরাবৃত্তি করতে হবে। যদি আপনি ইচ্ছা করেন তবে উক্ত নিয়ম প্রভৃতি চালিয়ে যেতে পারেন।

অনুরূপভাবে উদাহরণ সংগ্রহের কেন্দ্রের কর্মচারীরা এই লালা ও রক্ত সংগ্রহের জন্য আপনার বাড়ীতে আসিতে অথবা আপনাকে হাসপাতালে যাওয়ার জন্য গাড়ীর ব্যবস্থা করিবে। রক্ত ও লালা দিতে আপনার সামান্য অসুবিধা হইতে এই গবেষণায় অংশগ্রহণে আপনার কোন অসুবিধা বা সমস্যা নেই। আপনি ইচ্ছামত যে কোন প্রশ্ন জিজ্ঞাসা করিতে পারেন। এই গবেষণায় যাহারা দিয়াছে সাহায্য করিতে আপনি বাধ্য নহেন। আপনি ইচ্ছা করিলে মত পরিবর্তন করিতে পারেন। এতে করে আপনার এই প্রকল্প থেকে সরে গেলে আপনার কোন সমস্যার সৃষ্টি হবে না। সমস্ত তথ্যাবলীর গোপনীয়তা রক্ষা করা হবে এবং শুধু যাহারা এই প্রকল্পের সাথে জড়িত আছে, তাহারাই জানতে পারবে যে, আপনি আমাদের এই প্রকল্পে সাহায্য করেছেন।

<u>অংশগ্রহণ করার সম্মতি</u>

উল্লিখিত তথ্যাবলী আমি বুঝিয়াছি এবং যে কোন প্রশ্নমালার জিজ্ঞাসা করার সুযোগ পেয়েছি। আমি এখানে বলছি যে, গবেষণা প্রকল্পে সমস্ত উত্তর সঠিক জেনে দিয়েছি। আমি এই প্রকল্পে অংশগ্রহণ করতে সম্মত হলাম।

International Centre for Diarrhoeal Disease Research, Bangladesh

Memorandum

TO : Chairman, Research Review Committee

REF: BS-DMPA-PP

FROM : Dr. Brian Seaton

DATE: February 10,1982

SUBJECT : PROTOCOL #82-004

I refer to my protocol #82-004 entitled "Effects of Nutritional Status on the Pharmacokinetics of Depomedroxy Progesterone Acetate" which is due to be reviewed at the meeting of the RRC tomorrow, Thursday, the 11th of February.

I have just received some information from my colleagues in the Tenovus Institute, Cardiff which indicates that they have successfully completed studies showing that there is an excellent correlation between the levels of DMPA in saliva and in plasma. Several copies of the relevant * graphs are attached for your information. It should be noted that this information has been supplied to me in advance of publication of these results in the international journals. The effects of these new results is to make it unnecessary for us to distinguish between phase-1 and phase-2 of the protocol as originally intended. I have discussed this matter with Dr. S. D'Souza, The Scientific Programme Head, and with his approval I would recommend that the distingtion between phase-1 and phase-2 in this protocol be now eleminated. Although the correlation between plasma and salivary DMPA levels has been established we would still execute phase-1 of the protocol since the data thus obtained would be valuable supporting ~~evidence~~ evidence of the validity of our procedures and would almost certainly be required by the reviewers when the results were eventually submitted for publication in the international journals.

The practical consequences of eleminating the distingtion between phase-1 and phase-2 will be that we will conduct both phases simultaneously with an appropriate reduction in the number of subjects required.

I hope that this minor amendment and the improvement to the protocol will meet with the approval of the RRC. Should you require any further information I would be happy to supply it.

cc. Dr. S. D'Souza, Scientific Programme Head,
Community Services Research orking Group.

Enclo:-*